REMARKS

Claims 1-22 are currently pending in the application. In an Office Action dated July 30, 2004 ("Office Action"), the Examiner objected to claims 5-6 and 19-20, rejected claims 1-9 under 35 U.S.C. § 112, second paragraph for being indefinite, rejected claim 8 under 35 U.S.C. § 112, second paragraph, rejected claims 1,9,11-13, and 15 under 35 U.S.C. § 102(e) as being anticipated by Chu et al., U.S. Patent No. 6.249,593 B1 ("Chu"), rejected claims 1-2, 10, 13-16, and 22 under 35 U.S.C. § 103(a) as being unpatentable over Fitzgerald, et al., U.S. Patent No. 6,341,182 B1 ("Fitzgerald"), and indicated that claims 3, 4, 7, 17-18, and 21 would be allowable if rewritten in independent form. Applicants' representative wishes to than the Examiner for the conditional allowance of claims 3, 4, 7, 17-18, and 21, and will consider amending the claims as suggested by the Examiner should the following arguments fail to persuade the Examiner of the novelty and non-obviousness of the rejected claims. Applicants' representative has amended claims 5-6 and 19-20 to address the Examiner's objections. Applicants' representative has additionally amended claim 8 to partially address the Examiner's 35 U.S.C. § 112 rejection of claim 8. Applicants' representative respectfully traverses the 35 U.S.C. § 112, 35 U.S.C. § 102(e), and 35 U.S.C. § 103(a) rejections for reasons provided in the following paragraphs.

With regard to the Examiner's 35 U.S.C. § 112 rejection of claim 8, Applicants' representative observes that the term "chi0squared" represents an inadvertent typographical error, and has been amended to "chi-square." The phrase "chi-square distribution" is quite thoroughly discussed in the specification. For example, beginning on line 6 of page 15, the chi-squared distribution is discussed as follows:

> Using the above-described variance model, a threshold value, or $\hat{\sigma}^2_{max}$, can be estimated using an assumption that the following expression is distributed according to a χ^2 distribution with n-1 degrees of freedom, where n is the number of feature or feature background pixels:
>
> $$\frac{(n-1)\hat{\sigma}^2}{\sigma^2}$$

where σ^2 is the true feature or feature background variance under the assumption that the model is valid, and the feature or feature background is not an outlier

A representative χ^2 distribution is shown in Figure 9C, where the χ^2 distribution is expressed as follows:

$$f(y) = \begin{cases} \dfrac{y^{(v/2)-1} e^{-y/2}}{2^{v/2}\Gamma(v/2)}, y \geq 0, v \geq 0 \\ 0 \end{cases}$$

$$\text{where } \Gamma(v/2) = \int_0^\infty y^{(v/2)-1} e^{-y} dy$$

v = number of degrees of freedom

Please note that the phrase "chi-squared distribution" is equivalent to the mathematical phrase "χ^2 distribution" that employs the Greek letter "χ" raised to the power 2, or, in other words, squared. The equivalence of these two phrases is well known to those ordinarily skilled in data analysis and statistics. Furthermore, the term "chi-squared" is embodied in the C++-pseudocode variable name "chiSquaredXPoint" mentioned on line 5 of page 21 and included in the C++ pseudocode provided in the specification.

With regard to the 35 U.S.C. § 112, 35 U.S.C. § 102(e), and 35 U.S.C. § 103(a) rejections, Applicants' representative provides, for the Examiner's convenience, claim 1 below, with emphasis added, as representative of the novelty and non-obviousness of the currently claimed invention:

> 1. A method for identifying a non-uniform measured signal distribution in a region of a scanned image of a molecular array, the method comprising:
>
> providing a *variance model* for measured signal distributions within regions of the molecular array;
>
> determining a *variance* of measured signals within the region; and
>
> determining whether or not the region contains a non-uniform measured signal distribution by comparing the *determined variance of measured signals* within the region to the *variance model*.

Independent claim 15 includes similar language specifically directed to the variance to and variance models. Please note that Applicants clearly claim a variance model and a determined variance of measured signals. The term "variance" is not a casually

employed description of any type of mathematical characterization, but is, instead, a well-recognized statistical measure of the variability of data, and is well-described in the current application. For example, beginning on line 8 of page 11 of the specification, an embodiment of the present invention is discussed as follows, with emphasis added:

> An estimate of the *variance* of the per-pixel counts within the area of a digital representation of a molecular array corresponding to a feature or feature background is obtained as follows:
>
> $$S^2_{s_{net}} = \frac{1}{n-1}\sum_{i=1}^{n}\left(s_{net} - \bar{s}_{net}\right)^2$$
>
> $$where\ \bar{s}_{net} = \frac{1}{n}\sum_{i=1}^{n} s_{net},$$
>
> S = standard deviation, and
> n = the number of pixels within the feature or feature background
>
> Thus, the variance of pixel counts or pixel-based signal intensities within a feature or feature background can be straightforwardly calculated from the net signals obtained from the digital representation of the scanned image of a molecular array.
>
> In order to determine whether the pixel counts or pixel-based signal intensities within a feature or feature background are sufficiently uniform, the calculated *variance* "$S^2_{s_{net}}$" needs to be compared to a threshold value to determine whether or not the *calculated variance* "$S^2_{s_{net}}$" falls below the threshold value and therefore is acceptable. While current methods employ values measured from negative control features included within a molecular array, or depend on manual inspection of pixel count distributions, the present invention employs a calculated variance model to obtain the threshold value. In one embodiment of the present invention, *the calculated variance model "$\hat{\sigma}^2$" is a linear combination of three different, independent model variances:*
>
> $$\hat{\sigma}^2 = \hat{\sigma}^2_{\text{labeling and feature synthesis}} + \hat{\sigma}^2_{\text{counting}} + \hat{\sigma}^2_{\text{noise}}$$
>
> *The model variance* "$\hat{\sigma}^2_{\text{labeling and feature synthesis}}$" is the *variance* expected for non-uniformities associated with target-molecule labeling, feature synthesis, and other solution and surface and chemistry effects. *The model variance* "$\hat{\sigma}^2_{\text{counting}}$" is the *variance* expected in scanning measurement, or counting, error. The *model variance* "$\hat{\sigma}^2_{\text{noise}}$" is the expected *variance* due to electronic noise in the scanner, background-level signal noise produced by the glass substrate of the molecular array, and other such noise.

Please note the uses in the above-provided extract of the terms "variance" and "variance model." One explicit definition of the term "variance" is provided in the current

application in the above-quoted formula. The model variances are mentioned in the above extract, and are described in full mathematical detail in paragraphs of the specification following the above extracted portion of the specification, and include normal, binomial, and Poisson distributions – all well known statistical distribution models.

Applicants' representative has carefully read both Chu and Fitzgerald, and cannot find a single mention of suggestion of calculation of variance or use of variance models. For example, in the cited portions of Chu, Applicants' representative can find only a rather vague description of "computing a predefined mathematical function of the average density of the analyte region. The mathematical function may be as simple as subtracting the background density from the analyte density, or may be a considerable more complex function" on lines 46-48 of column 9. The variance is not an average density, and is not obtained by a simple subtraction. A generalized mention of mathematical functions used to compute averages cannot anticipate a specifically described and claimed method employing variance and variance models. Fitzgerald also not once mentions or suggests variance or variance models. Fitzgerald instead discloses a method for determining threshold values for pixel intensities, and mentions averaging pixel values (line 54 of column 1) or using predetermined percentages of highest and lowest pixel values (e.g. lines 29-31 of column2). Fitzgerald again discusses using an average pixel value in the formula on line 30 of column 6 and in neighboring text passages. But Fitzgerald does not once mention variance or variance models.

Claim 1 specifically claims "a method for identifying a non-uniform measured signal distribution in a region of a scanned image of a molecular array," but neither Fitzgerald or Chu are directed to scanned images of molecular arrays. Molecular arrays are described in great detail in the Background of the Invention section of the current application. Both Fitzgerald and Chu are concerned with processing images of multi-analyte sample trays.

In summary, Applicants clearly and explicitly claim, in claims 1 and 15, and in dependent claims that depend from them, a method and system, respectively, involving computing variances and comparing computing variances to variance models. Variances and variance models are described in great detail in the current application. The cited references neither disclose nor mention computing variances or employ variance models. Applicants' representative does not believe that either Fitzgerald, Chu, or Chu and Fitzgerald in combination teach, mention, or suggest Applicants' clearly claimed method.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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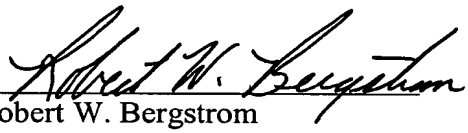

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